

REMARKS

In an Office Action mailed January 27, 2009, the Examiner in charge of the application stated the status of the claims. Applicants noted a small inconsistency in this statement of claims pending, considered or withdrawn: Claim 28 (withdrawn) was not listed among the pending or withdrawn claims. Claims 2, 3, 14, and 15 have been cancelled; Claims 1, 4-12, 25, and 28 are withdrawn from consideration as being drawn to non-elected subject matter; and Claims 13, 16-24, 26, and 27 are under consideration. The Examiner withdrew the novelty rejection in view of Applicants' previous response but reinstated an obviousness rejection from an Office Action dated September 27, 2007.

The Examiner rejected Claims 13, 16-24, 26 and 27 under 35 U.S.C. § 103(a) for alleged obviousness over Russell *et al.*, in view of Xu *et al.* Russell teaches applying strain with an apparatus to differentiate cells. Xu teaches human embryonic stem (ES) cells in feeder-free culture. In a March 25, 2008 response, Applicants emphasized that the skilled artisan would not use the apparatus to proliferate undifferentiated cells because Russell teaches using the apparatus to differentiate cells and, therefore, that one would not combine the apparatus with the undifferentiated hES cells to arrive at the claimed composition. In response, the Examiner alleged that Russell in combination with Xu teaches undifferentiated human ES cells in the apparatus and, therefore, make obvious Applicants' invention (Office Action, page 4, first paragraph). According to the Examiner, use of the apparatus provides no structural distinction to the composition and it matters not how the undifferentiated cells were produced (Office Action, page 4, second paragraph).

Russell in combination with Xu does not teach the claimed composition and is inconsistent with a composition that comprises embryonic stem cells and the straining apparatus. In fact, Russell would have had no reason to provide, undifferentiated cells in the strain-applying apparatus in their studies of myocytes or fibroblasts because, as Applicants demonstrate, embryonic stem cells remain undifferentiated in the apparatus. On the other hand, Russell was interested in differentiating myocytes or fibroblasts in specialized substrata by applying mechanical strain to myocytes or fibroblasts ([0008]; [0037]; [0108]; [0131]; [0145]; [0146]) but not to undifferentiated embryonic stem cells.

Russell does not teach a composition comprising embryonic stem cells. While Russell mentions that the myocytes or fibroblasts could be derived from embryonic stem cells ([0106]; [0108]), such derivations are entirely distinct laboratory processes that in no way suggest substituting embryonic stem cells for the Russell myocytes or fibroblasts in the apparatus. Assuming, *arguendo*, that Russell suggests such a substitution (an assumption that Applicants dispute), then Russell's goal would have been frustrated, as Russell would not have obtained the myocytes or fibroblasts of interest, for the reasons noted above. Further, a skilled artisan would have had no motivation to modify Russell to provide embryonic stem cells in the apparatus because Russell describes an apparatus that enhances differentiation, not one that maintains or proliferates undifferentiated embryonic stem cells. Still further, Russell fails to teach that the cells proliferate in the apparatus.

The noted gaps between the Russell disclosure and the Applicants' claims are simply too great to be bridged by a paper that describes only a feeder-free human embryonic stem cell culture. Applicants do not dispute Xu's teaching about culturing human embryonic stem cells as stated by the Examiner, but adamantly traverse the Examiner's suggestion that a skilled person would find any motivation to combine the Xu cells with the Russell apparatus. Absent more, the mere existence of a material (here, cultured human embryonic stem cells) cannot suggest all settings in which such material could or would be suitable. This goes to the very heart of "invention," and especially to the heart of invention where unexpected results are observed. The Examiner has shown no more than the existence of a feeder-free human embryonic stem cell culture, but improperly suggests that this alone suffices to suggest combining the culture with an apparatus that Russell showed as unsuited to maintain the embryonic stem cell culture. Where is the skilled person's incentive to combine these technologies? For the reasons noted above, it cannot come from Russell's mention that the differentiated cells in the apparatus can be separately derived from embryonic stem cells. Applicants maintain that the Examiner has not shown any reason to combine.

The Examiner alleged that "wherein more of the human ES cells ... are undifferentiated than in an otherwise comparable cell culture composition comprising an apparatus not configured to apply periodic strain to the matrix and the human ES cells" does not provide a structural limitation to the claimed invention. Applicants describe structural limitations above

that distinguish the invention from documents cited by the Examiner and remove the recited attribute from the claims so the issue is moot.

Reconsideration is respectfully requested.

Fees

No fee or extension of time is believed due, but should any fee or extension be due, in this or any subsequent response, please consider this to be a request to charge the fee to Deposit Account No. 17-0055 or a petition for the appropriate extension, and a request to charge the extension fee to the same Deposit Account.

Respectfully submitted,



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